

### REMARKS

Upon entry of the above amendments, this application will contain claims 1-9, 11-16, and 17-29 pending and under consideration. In this present Response, claims 1 and 13 have been amended; claims 10 and 17 have been canceled.

In the Office Action dated September 10, 2004, made final, claims 1-29 were rejected under 35 USC §103 over Wironen et al (US 2002/0076429, Wironen).

For the reasons discussed more fully below, it is believed that the claimed invention is patentably distinct from the cited reference. Withdrawal of all rejections and allowance of this application is respectfully requested.

#### Claim Rejections Under 35 USC §103

Claims 1-29 were rejected under 35 USC §103(a) over Wironen. The Applicants respectfully traverse the Examiner's rejection.

To advance the prosecution of this application, claims 1 and 11 have been amended to further define and claim that which the Applicants consider their invention. While it is acknowledged that amendments after final are not entered as a matter of right, it is believed that the above amendments should be entered. Claim 1 has been amended by inserting the substance of the matter recited in dependent claim 10, which has been canceled. Similarly, independent claim 13 has been amended by incorporating the substance of the matter recited in dependent claim 17, which has also been canceled. Since the claim amendments result in claims which were already pending in the case, no further searching should be required of the Examiner and the amendments should be entered.

Part of what the Applicants have done is to discover a solution to a problem that had heretofore been unknown. The Applicants have discovered that the inclusion of an osteoblast- and osteoclast-stimulating osteogenic factor in a paste-form composition including a resorbable paste carrier causes a rapid and premature resorption of the carrier. This rapid resorption of the carrier can diminish or eliminate the capacity of the paste-form composition to effectively stimulate and support new bone formation in a void filled with the composition. This is particularly the case in primates, including humans, in which the rate of new bone formation is relatively slow. (Application, page 7, lines 3-14.)

Part of what led the Applicants to this conclusion, was their surprising discovery that incorporation of lower amounts of an osteogenic material affords greater amounts of bone growth. (Application, Example 1, pages 21-23.) It was also noted that over time less calcification--not more--was observed for the paste formulations with higher amounts of the bone growth factor. (Id, page 22, lines 24-27.) Additionally, the Applicants discovered that the paste formulations having the most readily absorbable matrices i.e., gelatin pastes, a provided the poorest calcification performances. (Id, page 23, lines 2-6, and Fig. 2.) Therefore, Applicants theorized that bone morphogenic proteins stimulates both osteoblasts osteoclasts such that the resorbable carrier is quickly resorbed and can cause the performance of the composition to suffer to the extent that sporadic bone growth can be observed. (Id, page 12, lines 12-29.) This was born out to be true as outlined below.

The Applicants compared different paste compositions, which is detailed in Example 2 in the Application. (Id, pages 23-24.) In that study, three different paste compositions were examined for their ability to generate new bone growth, (1) gelatin and DMB (demineralized bone matrix), (2) gelatin, DMB and bone chips; and (3) gelatin, DMB, bone chips and a bone morphogenic protein, rhBMP-2. The results indicated that bone growth was observed for the first two paste compositions, i.e., those with gelatin, DMB; and gelatin, DMB and bone chips. However, no bone growth was observed with the third paste composition, i.e., that containing gelatin, DMB, bone chips and a bone morphogenic protein. This observation is in line with the Applicants' theory. No bone growth was observed due to the premature resorption of the carrier in the rhBMP-2-containing paste, leaving no matrix for bone ingrowth. Accordingly, the Applicants determined that incorporation of a substantial mineral component, greater than about 20%, in a BMP-containing paste in accordance with the claimed invention will provide a lasting matrix and scaffold for bone ingrowth, thus improving performance.

The Applicants believe that they have discovered the source of a problem and its solution to promote more rapid and complete bone growth. It is believed that the source of the problem and its solution are not obvious. (MPEP 2141.02.) Further, it is believed that no similar problem and therefore its source or cause was unknown prior the date of the Applicants' invention. Therefore, it could not be disclosed or taught in Wironen prior to the Applicants' discovery. In light of the above discussion, it is believed that the claimed invention is patentably distinct over the cited reference.

The Applicants also incorporate the prior response that they have discovered and used a result effective parameter that has not been previously known or discussed in the references. Specifically, the Applicants have determined that incorporation of effective inductive amounts of osteogenic factors such as bone morphogenic proteins stimulates the osteoclasts such that the resorbable carrier is quickly resorbed and can cause the performance of the composition to suffer to the extent that sporadic bone growth can be observed. (Application, page 12, lines 12-29.) In essence, the osteogenic factors stimulate both osteoblasts that induce bone growth as well as osteoclasts that induce bone absorption. This results in a weakened, incomplete healing or psuedoarthrosis at the defect site. The Applicants have determined that incorporating at least 20% by volume of a porous particulate mineral provides an effective scaffold for bone ingrowth to mitigate the potentiating effect of the osteoclast induction. This observation is a result effective parameter which has not been observed, described, or discussed in the prior art references and, in particular, not disclosed or discussed in the Wironen reference. Therefore, this variable cannot be optimized considering the prior art references. (MPEP §2144.05 II.) Therefore, the Applicants request that the rejections of the claims over Wironen be withdrawn and this application be allowed to issue with claims 1-9, 11-16, and 18-29.

### Conclusion

In view of the foregoing remarks, Applicants respectfully submit that the cited reference, either singly does not disclose or make obvious the claimed invention. Accordingly, reconsideration leading to withdraw of all the rejections under 35 U.S.C. §103 and passage of this application containing claims 1-9, 11-16, and 18-29 are respectfully requested. Additionally, the Examiner is invited to telephone the undersigned attorney if there are any questions about this submission or other matters, which may be addressed in that fashion.

Respectfully submitted,

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